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13. ABSTRACT (Maximum 200 words)

The concept of an area-minimizing surface has been used extensively to describe the morphologies of hydrated amphiphiles and block copolymers. These morphologies include lamellar, hexagonal, and the more complex bicontinuous cubic phases. In spite of the morphological similarities between certain block copolymers and hydrated amphiphiles there are of course some major differences. The stability of the two systems can be widely different. This distinction is now minimized by the successful introduction of methods to polymerize and even crosslink the phases of hydrated amphiphiles to greatly enhance their stability. The presence of the water domains in the polymerized nonlamellar phases, in particular the inverted hexagonal phase, are regions of well defined size and shape. This research is examining methods to create novel materials by selective use of these to (1) deposit metals and minerals or (2) isolate rod-like polymers. The major focus of the ongoing research is to extend the current state of the science to ascertain the potential and limits of a fundamentally new method for the synthesis of high value supramolecular composites.

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Research Problem

The well-defined water domains in polymerized nonlamellar phases of hydrated amphiphiles, such as the inverted hexagonal phase (H_{II}), affords the opportunity to create novel nanocomposites by the formation of polymers, metals, or minerals in the water channels. The H_{II} phase is composed of long cylindrical tubes of water in a hexagonal array, where the water cylinders are each surrounded by a monolayer of lipids.[1] Our laboratory has previously introduced a successful strategy for the polymerization of both H_{II} and bicontinuous cubic (Q_{II}) phases, that retains their morphology and stabilizes the assembly in a manner that enhances both the temperature range of the phase and its resistance to solubilization by organic solvents and surfactants.[2,3] Thus the lipid domains can be converted to poly(lipid) with a wide range of polymer properties, while leaving the water domains unperturbed for further elaboration. The major focus of this research is to extend the current state of the science to ascertain the potential of a fundamentally new method for the synthesis of nanocomposites. In effect this research seeks to exploit recent advances in the understanding of biological systems to create new synthetic materials.

Research Summary

A major part of the sponsored research has been the synthesis of polymerizable lipids that are designed to form the inverted hexagonal phase. This effort has been partly devoted to the preparation of materials for further study (as described below) as well as the development of new synthetic methodology for the more efficient synthesis of reactive dienoyl substituted lipids. The later has resulted in significant improvements in polymerizable lipid synthesis.[4,5] The selection of lipids for this research relies upon both the current knowledge of factors that affect the phase behavior of hydrated lipids, as well as our understanding of the polymerization of organized assemblies of lipids.[6] The state of knowledge is growing in both areas and we have successfully demonstrated that preformed nonlamellar phases of reactive dienoyl lipids can be polymerized to create stabilized supramolecular assemblies. The dienoyl group is useful for the proposed polymerization studies for the following reasons. First, it is known that dienoyl lipids may be polymerized by radical chain processes in the lamellar, L_α, phase. Lipids in the L_α phase exhibit rapid lateral diffusion, which facilitates the polymerization process in lipid assemblies. We have reported a series of systematic studies which provide new insights into the two-dimensional polymerizations of L_α phase.[6] Second, a comparative study of the polymerization of dienoyl amphiphiles in the L_α and the H_{II} phases revealed that these reactions are quite similar in both the rate and degree of polymerization.[7] Third, the polymerization of dienoyl lipids can be usefully initiated by photo, thermal, or redox chemistries. Fourth, the dienoyl group is a diene activated by the lipid acyl carbonyl and its

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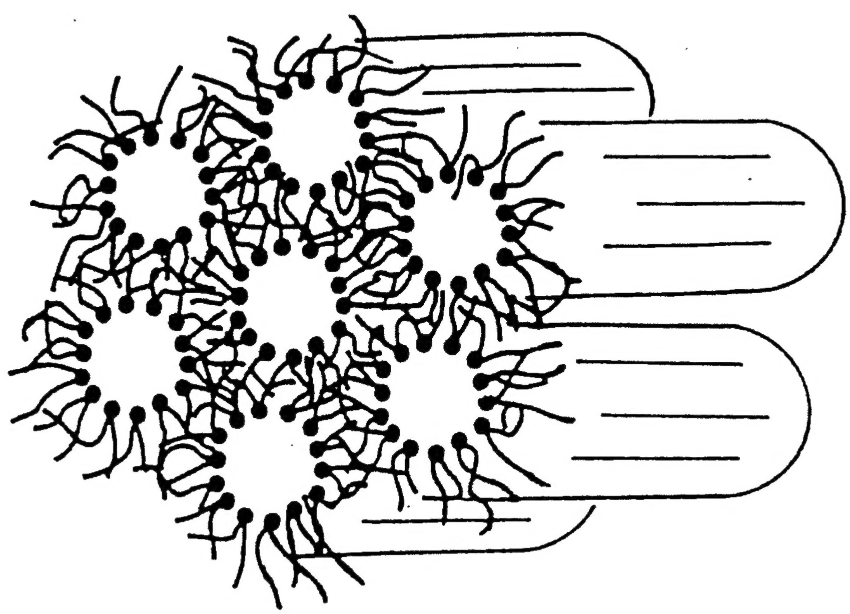
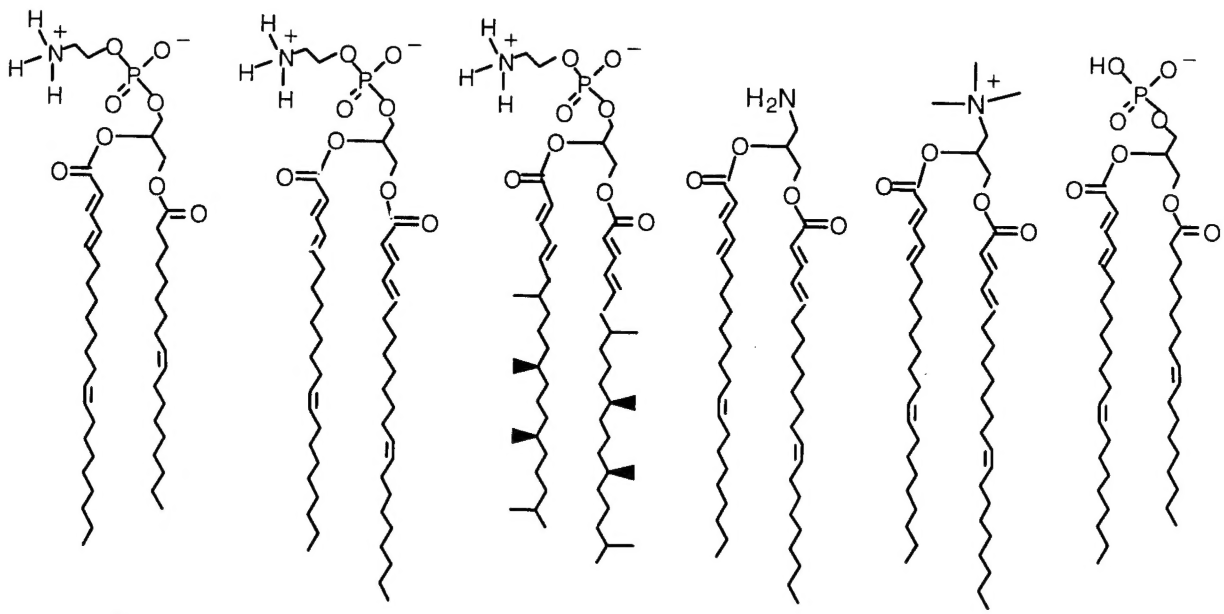
Figure 1. Schematic representation of the inverted hexagonal phase. The hydrophilic lipid head groups are represented by black dots and the hydrophobic lipid tails are represented by wavy lines. The unit cell of the inverted hexagonal phase is composed of a curved monolayer of lipids surrounding a column of water. The head group of the lipid interfaces with the water channel. The polymerization of the lipids described in this report occurs near the lipid head group in a manner that stabilizes each unit cell, but does not link the unit cells together.



polymerization results in minimum perturbation of the lipid hydrocarbon chain motions that are important for the maintenance of nonlamellar phases. In addition the rubber-like properties of poly(diene) appears to be well-suited to the highly curved surfaces of the H_{II} phase.



1 2 3 4 5 6

Compounds **1-6** are each dienoyl substituted lipids designed to form the H_{II} phase alone or in combination with one another.[1] Lipid **1** is a mono-substituted dienoyl PE (mono-DenPE) used for the formation of linear polymer chains within the unit cells of the H_{II} phase. In contrast lipid **2** is a bis-substituted dienoyl PE (bis-DenPE) used to crosslink the lipids within each unit cell of the H_{II} phase.[3] Lipid **3** is also a bis-DenPE, but with highly branched fatty acid chains.[5] This branching pattern provides a saturated chain alternative to the cis-double bonds in the other lipids (**1**, **2**) which are used to lower the temperature of the phase transition from lamellar to the H_{II} phase. Lipid **4** is a polymerizable amino lipid that can be combined in different quantities with lipid **2** to form the H_{II} phase, and provide binding sites for metallization (see below). Lipids **5** and **6** are polymerizable cationic and anionic lipid respectively, which can be combined in different molar amounts to control the surface charge at the interface of the lipid-water channels.

The polymerization of the H_{II} phase from the above lipids effectively yields a polymeric unit cell, i.e. a stabilized nanotube. The water channel within each tube provide interesting sites for the formation of organic-inorganic composites. It is already known

that both monolayers and bilayer assemblies are useful for the template directed growth of minerals or the geometrically controlled deposition of metals. We have used the nonpolymerizable dioleoylPE (DOPE) or the polymerizable lipid **2** to form the H_{II} phase for metallization experiments. Catalytic palladium particles can be deposited in the water channels of the H_{II} phase by the following procedure.[8] When either DOPE or lipid **2** is hydrated with pH 9 buffer, the ammonium head group is partially deprotonated (pK ~ 9) and about half of the lipids are anionic and the rest are zwitterionic. This condition favors the formation of a lamellar phase of these lipids, i.e. bilayer vesicles. Therefore 100 nm diameter bilayer vesicles of DOPE or lipid **2** are formed at pH 9. When a solution of tetraamine palladium chloride was added to the vesicles, the palladium (II) bound to some of the amine head groups on the exterior of the vesicles. It was reduced to form Pd (0) nanoparticles at the vesicle's surface. The vesicle suspension could then be converted to the H_{II} phase, by reducing the pH of the buffer to about 7. When these lipids become neutral (zwiterionic) the preferred phase at room temperature is the H_{II} phase. Consequently, the suspension aggregates and reorganizes into a H_{II} phase. After removal of the excess water, both ^{31}P-NMR and X-ray diffraction were used to demonstrate that the lipids and Pd particles were in the H_{II} phase. In order to more effectively control the number of nucleation sites for metallization we have recently prepared the polymerizable amino lipid **4**. This lipid is used in combination with other polymerizable zwitterionic lipids, such as **2**, to form the H_{II} phase with a specified number of readily metallated binding sites. Our studies indicate that this approach will make it possible to control the metallization process along the interior water channels of the H_{II} phase.

Lewis and McElhaney reported that the H_{II} phase could be formed from nearly equimolar mixtures of cationic and anionic lipids.[9] We have prepared polymerizable analogs of the cationic (**5**) and anionic (**6**) lipids, and found that they can be used to prepare the H_{II} phase, which can then be polymerized. As long as the net surface charge of the lipid mixture is nearly neutral the H_{II} phase can be formed at reasonable temperatures. Safinya and coworkers demonstrated that when a equimolar mixture of DOPE and a cationic lipid were combined with double stranded DNA the DNA was entrapped in the water channels of the H_{II} phase.[10] The electrostatic interactions between the quaternary ammonium group of the cationic lipid-and the phosphate groups of the DNA provide a strong association that maintains the structure of the H_{II} phase. In addition the charge neutralization of the anionic DNA and cationic lipids is important to H_{II} phase formation. By combining the observations of Lewis and McElhaney with those of Koltover et al. we have been able to prepare polymerizable H_{II} phases surrounding anionic polymers. In the first instance, we used lambda phage DNA as the polymer, which leads to the formation of individual DNA nanotubes, i.e. a DNA chain surrounded by a polymerized unit cell of the reactive lipids used to form the H_{II} phase. Morover, the polymer could be any polyelectrolyte, either anionic like DNA (using cationic lipids) or a cationic polymer (using anionic lipids). We

have prepared conducting polymers, such as poly(phenyleneethynylene), with side chains that will be functionalized to make them either cationic or anionic for use with the oppositisely charged polymerizable lipid. In this manner we expect that polymerized nanotube assemblies of polyelectrolyte and H_{II} phase lipids will exhibit strong photoemission as well as favorable electrical properties.

Each of these studies were pursued to extend the current state of knowledge in order to ascertain the potential and limits of a fundamentally new method for the synthesis of nanocomposite materials.

Manuscripts for Peer Reviewed Journals

Grudinin, A.; Arzberger, S.; O'Brien, D.F. "Efficient synthesis of polymerizale lipids for the formation and stabilization of organic zeolites", manuscript in revision.

Grudinin, A.; Srisiri, W.; Lee, Y-S.; O'Brien, D.F. "Synthesis of polymerizable lipids derived from phytol", manuscript in preparation.

Jeong, S.W.; O'Brien, D.F. "Solid state synthesis of polymerizable lipids", manuscript in preparation.

Arzberger, S.; Jeong, S.W.; O'Brien, D.F. "Stabilization of the unit cell of the inverted hexagonal phase", manuscript in preparation.

Scientific Personnel

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Mr. Steve Arzberger	Graduate student (4th yr)

Inventions

None

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